Remarks

Upon entry of the foregoing amendments, claims 37 – 56 are under consideration. Applicants have cancelled claims 31 – 36 and added new claims 37 – 56 to more clearly define the present invention. New claims 37 – 56 are directed to polypeptides based on SEQ ID NO:2 in general. More particularly, new claims 37 – 56 are directed to structural elements within the polypeptides of the present invention. Specifically, new claims 37 – 44 are directed to structural elements with Zins4, including the B chain, C peptide and the A chain. New claims 45 – 52 are directed to polypeptides which comprising the B chain, C peptide and A chain, as well as polypeptides which only contain the B chain and the A chain. New claims 53 – 56 are directed to compositions comprising a pharmaceutically acceptable carrier and the polypeptides of the present invention. Basis for these new claims can be found in the Specification as originally filed, and specifically in original claims 1 – 8 and 30, and at pg. 2, lines 13-19; pg. 3, lines 1-20; pg. 10, lines 7-28; and pg. 11, lines 5-11.

Applicants have amended the Specification at pg. 6 to remove the nucleic acid sequences used as examples of either a hypothetical "complementary sequence" or a hypothetical "contig" as they neither encompass the present invention nor are necessary to practice the present invention. Applicants have amended the Specification at pg. 10 to include a sequence identifier for the amino acid sequence Arg-X-X-Arg.

The present amendments add no new matter.

SEQUENCE COMPLIANCE

The Examiner has objected to the Specification as not being in compliance with the Sequence Rules under 37 C.F.R. §1.821(d).

Applicants have amended the Specification at pg. 6 to remove the nucleic acid sequences used as examples of either a hypothetical "complementary sequence" or a hypothetical "contig." These sequences were merely included as an exemplification of each term. These sequences are not necessary to practice the present invention.

Applicants have amended the Specification at pg. 10 to include identify the amino acid sequence Arg-X-X-Arg as SEQ ID NO:13. Applicants file concurrently herewith a replacement Sequence Listing in compliance with the Sequence Rules under 37 C.F.R. §1.821(d). The replacement Sequence Listing reflects the addition of new SEQ ID NO:13, as described above.

Accordingly, Applicants believe that the present objections are now moot.

THE §101 REJECTION

The Examiner has rejected claims 31 – 36 under 35 U.S.C. §101, alleging that the claimed invention has no apparent or disclosed specific and substantial credible utility, as the instant application does not disclose the biological role of the claimed protein/DNA or its significance.

Applicants traverse. Applicants respectfully submit that the rejection is contrary to both the law and the United States Patent Office's own examination guidelines. The application of these standards to biotechnology inventions is discussed in the January 5, 2001 Utility Examination Guidelines, which state:

> An invention has a well-established utility if a person of ordinary skill would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties...), and the utility is specific, substantial, and credible...

See e.g. Utility Examination Guidelines, 66 F.R. 4 at pg. 1098, §II.B.1(c)(1). Moreover, "[a] patent examiner must accept a utility asserted by an applicant unless the Office has sound scientific reasoning to rebut the assertion." *Id.*

Structural similarity with a compound that has a known therapeutic or pharmacological utility is routinely found to be indicative of a well-established utility and supportive of an assertion of therapeutic utility for a similar compound. *See e.g.*, M.P.E.P. 2107.03; *see also*, In re Jolles, 628 F.2d 1322, 206 U.S.P.Q. 885 (CCPA 1980). And, as discussed in detail in the January 5, 2001 Federal Register Notice of the United States Patent

Office's Utility Examination Guidelines:

> When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein. . . . [A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient.

See e.g. Utility Examination Guidelines, 66 F.R. 4 at pg. 1096.

Applicants contend that the Office has not established a *prima facie* showing of lack of utility, nor provided sound scientific reasoning to rebut the assertion of utility in the application. As detailed below, one of skill in the art upon reading the specification would appreciate that the Zins4 polypeptides of the present invention are useful because Zins4 is a member of the relaxin superfamily.

As stated in the Specification, the polypeptides of the present invention have "homology to the relaxin family." *See e.g.* Specification at pg. 9, lines 13-15. Specifically, these polypeptides share **numerous structural similarities** with the hormone relaxin. For instance, the polypeptides of the present invention contain a B chain-C peptide-A chain motif found in the relaxins. *Id* at pg. 9, line 36 through pg. 10, line 1. More specifically, the polypeptides of the present invention share a classical relaxin structure, known as the "cysteine motif," which is highly conserved in the B and A chains of relaxin. *Id* at pg. 9, lines 27-35. In fact, "[s]equence analysis indicates that the human polypeptide sequence (SEQ ID NO:2) is **structurally equivalent** to other members of the [relaxin] family." *Id* at pg. 10, lines 5-6. Further, the length of the B chain, C peptide and A chain correspond closely to those of relaxin itself. *Id* at pg. 10, line 7 through pg. 11, line 15. Most importantly, the polypeptides of the present invention contain a R-x-x-x-R-x-x-I motif in the middle of the B-chain (starting at amino acid residue 37 (Arg) through residue 44 (Ile) of SEQ ID NO:2). This motif has been determined to be "**essential for relaxin receptor binding**." *See e.g.*, Bathgate *et al.*, *J. Bio. Chem.* 227:2 1148-1157 (2001) (cited in the June 12, 2002 Information Disclosure Statement as reference "A3") (*emphasis added*); *see also*, Specification at pg. 9, lines 31-35. In fact, Zins4 and relaxin *alone* share this B chain motif. These structural characteristics are well known in the art and are recognized as defining and directing relaxin's biological function(s). The presence of these

structural similarities would lead one of ordinary skill in the art to conclude that the polypeptides of the present invention are closely related to relaxin and consequently are more likely than not to have a substantially similar biological function as relaxin.

Furthermore, relaxin has a well-known and established biological function and many well-known utilities generally associated with female reproductive tract physiology. *See e.g.*, Bathgate *et al.*, *J. Bio. Chem.* 227:2 1148-1157 (2001). Specifically, relaxin has been shown to have utility in its ability to inhibit myometrial contractions, to stimulate remodeling of the connective tissue and to induce softening of the tissues of the birth canal. *Id* at pg. 1148. Relaxin has also demonstrated utility by its ability to breakdown of collagen, one of the main components of connective tissue. *Id.*

And, as acknowledged by the Examiner in her December 19, 2002 Office Action, Applicants have asserted a number of utilities which directly related to Zins4 application in female reproductive tract physiology, including contractility of tissues such as myometrial. *See e.g.* Specification at pg. 44, lines 13-37. Thus, one skilled in the art, in light of Zins4 obvious homology to relaxin, would immediately recognize and appreciate that the polypeptides of the present invention are useful in the same manner that relaxin itself is useful. Accordingly, one skilled in the art would immediately recognize the polypeptides of the present invention have a "real world use" that is specific, substantial and credible.

The Examiner has stated that the "instant claims are drawn to a protein (and compositions thereof) of as yet undetermined function or biological significance" and consequently, the "instant specification does not disclose a credible 'real world' use. *See e.g.,* December 19, 2002 Office Action at pg. 4.

Applicants disagree. Zins4 does indeed have an established and recognized biological function and significance. As discussed in detail above, Applicants have disclosed a biological function(s) for the polypeptides of the present invention. The presence of the disclosed structural similarities of Zins4 and relaxin would lead one of ordinary skill in the art to conclude that the polypeptides of the present invention are part of the relaxin family of proteins and consequently are more likely than not to share relaxin's well-known biological function(s). Furthermore, Bathgate *et al.* further substantiated the biological function of Zins4. Specifically, they used the

identical polypeptide, designated as "*H3* relaxin," which is disclosed in the present application as Zins4 (SEQ ID NO:2) to determine biological function of the polypeptide:

> Therefore, our data provide conclusive evidence that this novel peptide retains the structural features necessary for interaction with, and activation of, relaxin receptors and can therefore be termed a "relaxin."

See e.g., Bathgate *et al.* at pg. 1156.

Applicants assert that the polypeptides of the present invention would be recognized by one skilled in the art as having actual and specific significance. Applicants also assert that one skilled in the art would immediately recognize that the polypeptides of the present invention have a well-known biological function based on the surrounding art and the structural similarities of these polypeptides to relaxin. Thus, Applicants assert that the present Application does indeed disclose a credible "real world" use for the claimed polypeptides.

Based on the foregoing, it is clear that Examiner's assertions that the "claimed invention has no apparent or disclosed specific and substantial credible utility", as the instant application "does not disclose the biological role of the claimed protein/DNA or its significance" are unfounded. New claims 37 – 56 are indeed supported by a well-established and specific and substantial credible utility as described above. This is more than 35 U.S.C. §101 requires. The Office has not established a *prima facie* showing of lack of utility, nor sound scientific reasoning to rebut the assertions of utility in the application. Consequently, Applicants request that the Examiner withdraw the present rejection under 35 U.S.C. §101.

THE §112, FIRST PARAGRAPH REJECTION

The Examiner has rejected claims 31 – 36 under 35 U.S.C. §112, first paragraph, alleging that the Specification fails "to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C.

Applicants traverse. Applicants have indeed taught how to use the instant invention. As discussed above, Applicants have shown that the polypeptides of the present invention share numerous structural similarities with relaxin and, in fact, have been classified by those skilled in the art as being relaxins. Consequently, Applicants have shown a biological activity for the

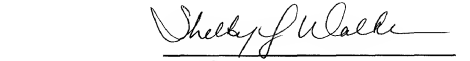
polypeptides of the present invention. Thus, Applicants assert that the Specification more than adequately teaches how to use the present invention.

Accordingly, Applicants maintain that they have indeed asserted a specific and substantial credible utility and well-established utility for the claimed polypeptides. The Zins4 polypeptides of the present invention are useful, and therefore one of skill in the art could make and use the invention. Consequently, Applicants request that the Examiner withdraw the rejection of claim 11 under 35 U.S.C. §112, first paragraph.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the Application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



Dated: June 19, 2003

Shelby J. Walker, Reg. No. 45,192
Attorney for Applicants
c/o ZYMOGENETICS, INC.
1201 Eastlake Avenue East
Seattle, Washington 98102-3702
Tel: (206) 442-6558
Fax: (206) 442-6678

Enclosures:
Petition and Fee for Extension of Time (in duplicate)
Amendment Fee Transmittal (in duplicate)
Postcard

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